REMARKS

In the Office Action of September 14, 2001, Claims 1 - 8 were rejected. No claim was allowed. In response, new Claims 9 - 30 are added to the application. Reexamination and reconsideration are respectfully requested in view of the foregoing amendments and the following remarks.

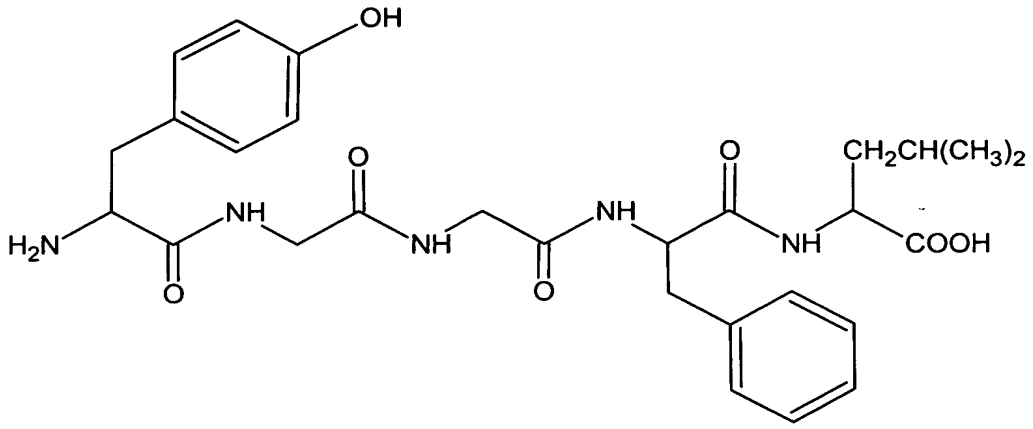
Rejection of Claims 1 - 8 under 35 U.S.C. §112, first paragraph

Claims 1 - 8 were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter that is not enabled by the specification. The Examiner alleges that the specification, while being enabling for peptides, proteins, enzymes and amino acid derivatives, does not provide enablement for all compounds having free amino groups. The Examiner takes the position that to claim all compounds having a free amino group is to claim too broad coverage for the applicant's invention.

This rejection is respectfully traversed. As described in the present specification (see page 3, lines 31-32), there is no specific restriction as to the compounds having a free amino group to be used in the present invention. Any compound can be used so long as it has a free amino group.

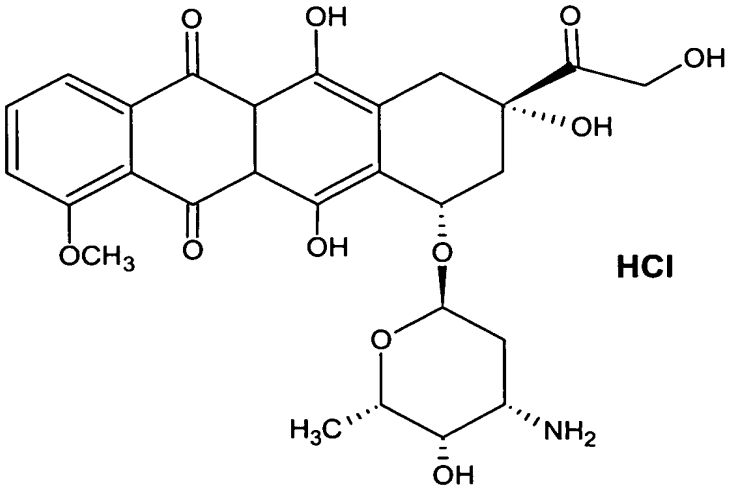
As an example, the Applicants conducted an experiment according to the present invention involving two distinctly different compounds, Enkephalin (leucine-enkephalin) and doxorubicin hydrochloride. Enkephalin (leucine-enkephalin,

Tyr-Gly-Gly-Phe-Leu) is a pentapeptide having a free amino group in its structure (see below).



As described in the experiment in the attached Declaration of Yasuki Kato, lactose reacts with enkephalin, to give a reaction product (product-A) in a weakly basic solution at 40°C with the passage of time (see Table A). Lowering of the pH of the mixture from 7.9 to 5.5 (a weakly acidic condition) caused rapid and almost complete release of lactose from product-A (see table B).

Likewise, a pharmaceutical compound, Doxorubicin hydrochloride has a free amino group in its structure (see below).



In the experiment described in the attached declaration, lactose reacts with Doxorubicin hydrochloride, to give a reaction products (product-B, product-C, product-D) in a weakly basic solution at 40°C with the passage of time (see Table C). Lowering of the pH of the mixture from 7.3 to 5.5 (a weakly acidic condition) caused rapid release of lactose from product-B (see table D).

These results show that compounds having a free amino group (for example, Enkephalin, Doxorubicin hydrochloride) react with a sugar having the reducing power and the obtained products are capable of rapidly releasing the compound having a free amino group. Thus, it is demonstrated that the claimed invention is enabled so long as a compound having a free amino group is used. It is therefore respectfully submitted that one skilled in the art could have made and used the claimed invention without undue experimentation.

Accordingly, withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

Rejection of Claims 1 - 4 under 35 U.S.C. §102(b) over Katsukiyo

Claims 1 - 4 were rejected under 35 U.S.C. §102(b) as anticipated by Katsukito (JP 7-61999). The Examiner alleges that Katsukito teaches a sugar-modified protein obtained when lactose-lactone is reacted with a protein, and that it also describes using insulin as the protein. The Examiner takes the position that the reference inherently teaches that a free

protein can be quickly separated through changes in pH.

This rejection is respectfully traversed. JP 7-61999 (Katsukiyo) discloses a sugar-modified protein obtained when lactose-lactone is reacted with a protein (in JP 7-61999, a protein is a compound having a free amino group). However, the sugar-modified protein shown in JP 7-61999 has the amide bond (-CO-NH-).

It is well known that the amide bond is quite stable and does not rapidly cleave to release a compound having a free amino group in response to changes in pH (see "Reactivity Chart 9. Protection for the Amino Group: Amides" (pp. 740-743) in PROTECTIVE GROUPS IN ORGANIC SYNTHESIS, edited by JOHN WILEY & SONS, INC., a copy of several pages enclosed herewith. Letters "H", "M", "L", and "R" in the Reactivity Chart 9 are defined in page 706, respectively.

A severe reaction condition (for example, pH 1, 100°C) is necessary to cleave the amide bond to release a compound having a free amino group, and thus a sugar-modified protein shown in JP 7-61999 does not rapidly release a compound having a free amino group only in response to changes in pH. Accordingly, JP 7-61999 does not disclose the claimed invention.

Accordingly, it is respectfully submitted that Claims 1 - 4 are not anticipated by Katsukiyo.

Rejection of Claim 1 - 8 under 35 U.S.C. §103(a) over Katsukito in view of Masashi

Claims 1 - 8 were rejected under 35 U.S.C. §103(a) over

Katsukito in view of Masashi (JP 9-263579) The Office Action alleges that Katsukito teaches a sugar-modified protein obtained when lactose-lactone is reacted with a protein, and that it also describes using insulin as the protein. The Examiner takes the position that the reference inherently teaches that a free protein can be quickly separated through changes in pH. The Examiner acknowledges that Katsukiyo does not teach medicines made by enclosing a drug make from protein into a micro-globule, ribosome, emulsion or other carrier. The Examiner alleges that Masashi et al teach medicines made by enclosing a drug make from protein into a micro-globule, ribosome, emulsion or other carrier. The Examiner takes the position that it would have been obvious to make the medicine by enclosing the sugar-modified protein of Katsukiyo into the known carrier of Masahi.

This rejection is traversed. JP 7-61999 does not disclose or suggest the claimed invention (as discussed above). JP 9-263579 also does not disclose nor suggest a pharmaceutical preparation capable of rapidly releasing a compound having a free amino group in response to changes in pH. Thus, it is not obvious to a person of ordinary skill in the art to make the pharmaceutical preparation claimed in the present application over JP 7-61999 in view of JP 9-263579. Accordingly, it is respectfully submitted that Claims 1 - 8, and new claims 9 - 30 would not have been obvious over Katsukito and Masashi, alone or in combination.

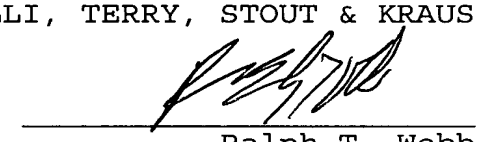
Conclusion

In view of the foregoing amendments and remarks, it is respectfully submitted that Claims 1 - 8 and new Claims 9 - 30 are in condition for allowance. Favorable reconsideration is respectfully requested.

Should the Examiner believe that anything further is necessary to place this application in condition for allowance, the Examiner is requested to contact applicants' undersigned attorney at the telephone number listed below.

Kindly charge any additional fees due, or credit overpayment of fees, to Deposit Account No. 01-2135 (506.40278X00).

Respectfully submitted,
ANTONELLI, TERRY, STOUT & KRAUS



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Enclosures:
1) Declaration of Yasuki Kato
2) Greene, Wuts, Eds., PROTECTIVE GROUPS IN ORGANIC SYNTHESIS, John Wiley & Sons, Inc., 1999, "Reactivity Chart 9. Protection for the Amino Group: Amides" (selected pages, including pp 740-743 and 706.) w/ PTO Form 1449